

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
PATENT APPLICATION EXAMINING OPERATIONS

Appl. No. : 10/516,405 Confirmation No. 2828  
Applicant : Demmer et al.  
Filed : November 30, 2004  
Title: Membrane, Device And Method For  
Removing Proteases From Liquids  
TC/A.U. :  
Examiner : Holland, Tamala D.  
Docket No. : 3568.0099  
Customer No. : 00152

**RESPONSE TO NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 USC 371**

1600 ODS Tower  
601 S.W. Second Avenue  
Portland, OR 97204  
(503) 227-5631

July 6, 2005

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

Applicant submits the following in response to the above-identified Notification dated June 27, 2005 (copy enclosed).

In the Notification, the current translation of the application into English is stated to be defective for the supposed reason that the number of claims in the International Application and the number of claims in the translation are not the same. The Office is respectfully submitted to be in error.

Appl. No. 10/516,405

Response to Notification Of Missing Requirements dated July 6, 2005

Specifically, attached hereto as Exhibit 1 is the cover page of the International Application and the two pages (12 and 13) containing the claims of that Application. Note that the total number of claims is 13.

Attached hereto as Exhibit 2 is a translation of pages 12-13 of the International Application, the said pages containing the claims of said Application. Note that the total number of claims in the English translation is also 13.

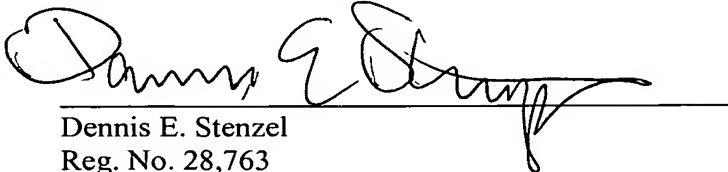
Accordingly, the number of claims in the International Application and the number of claims in the translation are the same.

It appears that the formalities Examiner in charge of this application has erroneously assumed that the substitute specification filed with this application was the English translation of the International Application. Note that the claims for the substitute specification fall on pages 8-9 of the substitute specification and contains 15 claims, two of which are multiple dependent claims.

Under the circumstances, withdrawal of the Notification of Missing Requirements Under 35 USC 371 is respectfully requested.

Respectfully submitted,

Chernoff, Vilhauer, McClung & Stenzel, LLP



Dennis E. Stenzel  
Reg. No. 28,763  
Tel No.: (503) 227-5631

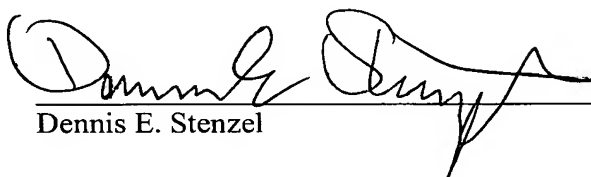
Appl. No. 10/516,405

Response to Notification Of Missing Requirements dated July 6, 2005

### CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450.

July 6 '05  
Date

  
Dennis E. Stenzel



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Page 1 of 2  
JUN 30 2005 35b

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CHERNOFF, VILHAUER,  
MCCLUNG & STENZEL

U.S. APPLICATION NUMBER NO.	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
10/516,405	Wolfgang Demmer	DES: 3568.0099

INTERNATIONAL APPLICATION NO.
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PCT/EP03/06366

I.A. FILING DATE	PRIORITY DATE
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06/17/2003

07/11/2002

152

CHERNOFF, VILHAUER, MCCLUNG & STENZEL  
1600 ODS TOWER  
601 SW SECOND AVENUE  
PORTLAND, OR 97204-3157

DES  
Docketed: 8/27/05

CONFIRMATION NO. 2828

371 FORMALITIES LETTER



\*OC000000016340369\*

Reminder: \_\_\_\_\_

By: *Jg*

Date Mailed: 06/27/2005

## NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C. 371 IN THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as a Designated / Elected Office (37 CFR 1.495).

- Copy of the International Application filed on 11/30/2004
- Copy of the International Search Report filed on 11/30/2004
- Information Disclosure Statements filed on 01/21/2005
- Oath or Declaration filed on 11/30/2004
- Request for Immediate Examination filed on 11/30/2004
- U.S. Basic National Fees filed on 11/30/2004
- Substitute Specification filed on 11/30/2004
- Assignment filed on 11/30/2004
- Priority Documents filed on 11/30/2004
- Power of Attorney filed on 06/06/2005

The following items **MUST** be furnished within the period set forth below in order to complete the requirements for acceptance under 35 U.S.C. 371:

- Translation of the application into English. Note a processing fee will be required if submitted later than 30 months from the priority date.
- Translation of the application into English. The current translation of the application into English is defective as described below. Note a processing fee will be required if submitted later than 30 months from the priority date.
  - ➔ The number of claims in the International Application and the number of claims in the translation are not the same.
- Processing fee for providing the translation of the application and/or the Annexes later than 30 months from the priority date (37 CFR 1.492(f)).

**SUMMARY OF FEES DUE:**

Total additional fees required for this application is **\$130** for a Large Entity:

- **\$130** for English translation surcharge required.

**ALL OF THE ITEMS SET FORTH ABOVE MUST BE SUBMITTED WITHIN TWO (2) MONTHS FROM THE DATE OF THIS NOTICE OR BY 32 MONTHS FROM THE PRIORITY DATE FOR THE APPLICATION, WHICHEVER IS LATER. FAILURE TO PROPERLY RESPOND WILL RESULT IN ABANDONMENT.**

The time period set above may be extended by filing a petition and fee for extension of time under the provisions of 37 CFR 1.136(a).

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

*A copy of this notice **MUST** be returned with the response.*

TAMALA D HOLLAND

Telephone: (703) 308-9140 EXT 209

**PART 1 - ATTORNEY/APPLICANT COPY**

U.S. APPLICATION NUMBER NO.	INTERNATIONAL APPLICATION NO.	ATTY. DOCKET NO.
10/516,405	PCT/EP03/06366	DES: 3568.0099

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES  
PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum  
Internationales Büro



(43) Internationales Veröffentlichungsdatum  
22. Januar 2004 (22.01.2004)

PCT

(10) Internationale Veröffentlichungsnummer  
**WO 2004/007069 A1**

(51) Internationale Patentklassifikation<sup>7</sup>: **B01J 20/32**,  
B01D 15/00, 69/02, C12N 9/50, C07K 14/81

(21) Internationales Aktenzeichen: PCT/EP2003/006366

(22) Internationales Anmeldedatum:  
17. Juni 2003 (17.06.2003)

(25) Einreichungssprache: Deutsch

(26) Veröffentlichungssprache: Deutsch

(30) Angaben zur Priorität:  
102 31 574.4 11. Juli 2002 (11.07.2002) DE

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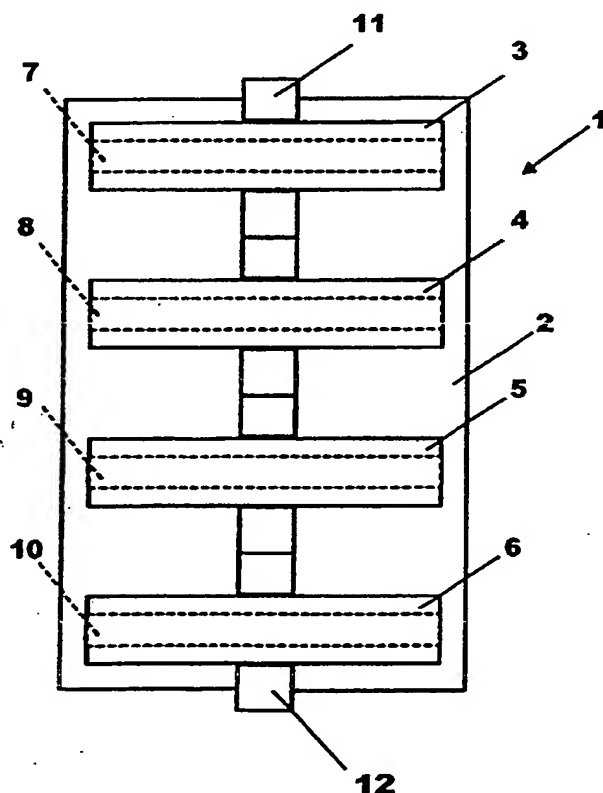
(81) Bestimmungsstaaten (national): AL, AM, AT, AU, AZ,  
BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES,  
FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP,  
KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,  
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL,  
TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW.

(84) Bestimmungsstaaten (regional): ARIPO-Patent (GH,  
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),

[Fortsetzung auf der nächsten Seite]

(54) Title: MEMBRANE, DEVICE AND METHOD FOR REMOVING PROTEASES FROM LIQUIDS

(54) Bezeichnung: MEMBRAN, VORRICHTUNG UND VERFAHREN ZUM ENTFERNEN VON PROTEASEN AUS FLÜS-  
SIGKEITEN



(57) Abstract: The invention relates to a membrane and device for removing proteases from liquids, particularly from biological liquids and pharmaceutical solutions, comprised of a microporous membrane body, whereby inhibitors that selectively bind proteases are coupled to the membrane body by chemically activated groups. The invention also relates to a method for removing proteases from liquids, particularly from biological liquids and pharmaceutical solutions, by microfiltration involving the use of microporous activated membranes, whereby inhibitors are coupled to the membranes by chemically activated groups, by means of which the proteases are removed by selective binding.

(57) Zusammenfassung: Membran und Vorrichtung zum Entfernen von Proteasen aus Flüssigkeiten, insbesondere aus biologischen Flüssigkeiten und pharmazeutischen Lösungen, bestehend aus einem mikroporösen Membrankörper, wobei Proteasen selektiv bindende Inhibitoren durch chemisch aktivierte Gruppen an den Membrankörper angekoppelt sind. Verfahren zum Entfernen von Proteasen aus Flüssigkeiten, insbesondere aus biologischen Flüssigkeiten und pharmazeutischen Lösungen, durch Mikrofiltration mit mikroporösen aktivierten Membranen, wobei an die Membranen Inhibitoren über chemisch aktivierte Gruppen angekoppelt werden, durch die die Proteasen durch selektive Anbindung entfernt werden.

## 5 Patentansprüche

1. Membran zum Entfernen von Proteasen aus Flüssigkeiten, bestehend aus einem mikroporösen Membrankörper, **dadurch gekennzeichnet**, dass Proteasen selektiv bindende Inhibitoren durch chemisch aktivierte Gruppen an den Membrankörper (7, 8, 9, 10) angekoppelt sind.

2. Membran nach Anspruch 1, **dadurch gekennzeichnet**, dass ein saure Proteasen bindender Inhibitor an den Membrankörper (7) angekoppelt ist.

3. Membran nach Anspruch 2, **dadurch gekennzeichnet**, dass Pepstatin an den Membrankörper (7) angekoppelt ist.

4. Membran nach einem der Ansprüche 1 bis 3, **dadurch gekennzeichnet**, dass ein Metallo-Proteasen bindender Inhibitor an dem Membrankörper (8) angekoppelt ist.

5. Membran nach Anspruch 4, **dadurch gekennzeichnet**, dass Bestatin, Diprotin oder EDTA an den Membrankörper (8) angekoppelt ist.

6. Membran nach einem der Ansprüche 1 bis 5, **dadurch gekennzeichnet**, dass ein Cystein-Proteasen bindender Inhibitor an den Membrankörper (9) angekoppelt ist.

7. Membran nach Anspruch 6, **dadurch gekennzeichnet**, dass Antipain, Chymostatin, Leupeptin oder E64 an den Membrankörper (9) angekoppelt ist.

8. Membran nach einem der Ansprüche 1 bis 7, **dadurch gekennzeichnet**, dass ein Serin-Proteasen bindender Inhibitor an den Membrankörper (10) angekoppelt ist.

5 9. Membran nach Anspruch 8, **dadurch gekennzeichnet**, dass TLCK oder p-Aminobenzamidin an den Membrankörper (10) angekoppelt ist.

10 10. Vorrichtung zum Entfernen von Proteasen aus biologischen Flüssigkeiten und pharmazeutischen Lösungen mit einer Mehrzahl in Reihe geschalteter Membranen, **dadurch gekennzeichnet**, dass die Membranen (3, 4, 5, 6) nach einem der Ansprüche 1 bis 9 ausgebildet sind.

15 11. Vorrichtung nach Anspruch 10, **dadurch gekennzeichnet**, dass die einzelnen Membranen (3, 4, 5, 6) jeweils einen Membrankörper (7, 8, 9, 10) mit einem anderen angekoppelten Inhibitor aufweisen.

20 12. Vorrichtung nach Anspruch 10 oder 11, **dadurch gekennzeichnet**, dass die Membranen (3, 4, 5, 6) in ein zur sequentiellen Durchströmung der Membranen (3, 4, 5, 6) geeignetes Gehäuse (2) eingebaut sind.

25 13. Verfahren zum Entfernen von Proteasen aus biologischen Flüssigkeiten und pharmazeutischen Lösungen durch Mikrofiltration mit mikroporösen aktivierten Membranen, **dadurch gekennzeichnet**, dass an die Membranen (3, 4, 5, 6) Inhibitoren über chemisch aktivierte Gruppen angekoppelt werden, durch  
30 die die Proteasen durch selektive Anbindung entfernt werden.





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## TRANSLATOR'S DECLARATION

*I, Stephen V. Vitek, technical translator and manager of PatentTranslators.com, 1304 False Creek Way, Chesapeake, VA 23322, hereby certify that I am a technical translator fluent in the German and English languages, as well as a member in good standing of the American Translators Association, National Capital Area Translators Association, Northern California Translators Association, etc., and that my translation of PCT Patent Application No. WO 2004/007069 A1 (MEMBRANE, DEVICE AND METHOD FOR REMOVING PROTEASES FROM LIQUIDS) is to the best of my knowledge and ability a true and faithful translation of this document in the German language into English.*

*Signed in Chesapeake, Virginia, on November 2, 2004.*

STEPHEN V. VITEK, TECHNICAL TRANSLATOR

EXHIBIT 2

## Patent Claims

1. A membrane for removing proteases from liquid, comprising a microporous membrane body, **characterized by the fact** that inhibitors binding selectively with proteases are coupled with chemically activated groups to the membrane bodies (7, 8, 9, 10).
2. The membrane according to claim 1, **characterized by the fact** that an inhibitor binding with acidic proteases is coupled to the membrane body (7).
3. The membrane according to claim 2, **characterized by the fact** that pepstatin is coupled to the membrane body (7).
4. The membrane according to claim 1 to 3, **characterized by the fact** that an inhibitor binding with metalloproteases is coupled to the membrane body (8).
5. The membrane according to claim 4, **characterized by the fact** that bestatin, diprotin or EDTA is coupled to the membrane body (8).
6. The membrane according to claim 1 through 5, **characterized by the fact** that an inhibitor binding with cysteine proteases is coupled to the membrane body (9).
7. The membrane according to claim 6, **characterized by the fact** that antipain, chymostatin, leupeptin or E64 is coupled to the membrane body (9).

[page 13]

8. The membrane according to claim 1 through 7, **characterized by the fact** that an inhibitor binding with serine proteases is coupled to the membrane body (10).
9. The membrane according to claim 8, **characterized by the fact** that TLCK or p-aminobenzamidine is coupled to the membrane body (10).
10. Device for removing proteases from biological liquids and pharmaceutical solutions with a plurality of connected membranes, **characterized by the fact** that the membranes (3, 4, 5, 6) are constructed according to one of the claims 1 through 9.
11. Device according to claim 10, **characterized by the fact** that each of the individual membranes (3, 4, 5, 6) is provided with a membrane body (7, 8, 9, 10) having another coupled inhibitor.
12. The device according to the claim 10 or 11, **characterized by the fact** that the membranes (3, 4, 5, 6) are built into a suitable housing (2) enabling a sequential flow through the membranes (3, 4, 5, 6).
13. A method for removing proteases from biological liquids and pharmaceutical solutions with microfiltration using microporous activated membranes, **characterized by the fact** that the inhibitors are coupled with chemically activated groups to the membranes (3, 4, 5, 6), wherein the proteases are removed with selective binding.